

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : James A. Laugharn, Jr. et al. Art Unit : Unknown
Serial No. : To be assigned Examiner : Unknown
Filed : July 9, 2001
Title : PRESSURE-CONTROLLED NUCLEIC ACID HYBRIDIZATION

Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Prior to examination, please amend the application as follows:

In the specification:

Replace the paragraph beginning at page 1, line 6 with the following rewritten paragraph:

-- This application is a continuation of U.S. Application No. 09/035,652, filed March 5, 1998, which claimed the benefit of U.S. Provisional Application No. 60/076,478, filed March 2, 1998, and of International Application No. PCT/US97/11198, filed July 1, 1997. --

In the claims:

Cancel claims 1-16.

Add claims 17-23.

-- 17. A nucleic acid amplification method, comprising:

(1) providing a sample vessel and temperature and pressure controllers for the vessel;

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(2) providing a first nucleic acid to be amplified, a nucleic acid primer that is at least partially complementary to the first nucleic acid, a DNA polymerase, and four deoxyribonucleoside triphosphates; wherein the primer has a nucleotide sequence that hybridizes to an internal nucleotide sequence in the first nucleic acid, the primer capable of being extended at least one nucleotide by the polymerase using the first nucleic acid as a template;

(3) increasing the temperature in the vessel to a temperature effective to cause denaturation of the first nucleic acid;

(4) increasing pressure in the vessel to a pressure above ambient pressure that allows hybridization between the denatured first nucleic acid and the primer; and

(5) allowing the DNA polymerase to extend the primer using the denatured first nucleic acid as a template, thereby making a copy of a least part of the first nucleic acid.

18. The method of claim 17, further comprising:

(6) decreasing pressure to a pressure at which the first nucleic acid again dissociates; and

(7) repeating steps (4)-(6) to further amplify the first nucleic acid.

19. The method of claim 17, wherein the primer is labelled.

20. A nucleic acid amplification method, comprising:

(1) providing a sample vessel and temperature and pressure controllers for the vessel;

(2) providing a first nucleic acid primer, a second nucleic acid primer, a target nucleic acid to be amplified, and a DNA ligase; wherein the first and second primers are at least partially complementary to the target nucleic acid and hybridize to adjacent sequences on the target nucleic acid;

(3) increasing the temperature in the vessel to a temperature effective to cause denaturation of the target nucleic acid;

(4) contacting the primers and denatured target nucleic acid within the vessel at a pressure above ambient pressure that is effective to allow hybridization between the primers and the denatured target nucleic acid; and

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(5) allowing the ligase to ligate the two primers, thereby making a copy of at least part of the target nucleic acid.

21. The method of claim 20, further comprising:

(6) decreasing pressure to a pressure at which the target nucleic acid again dissociates;

and

(7) repeating steps (4)-(6) to further amplify the target nucleic acid.

22. The method of claim 20, wherein the first primer is labelled.

23. A method of hybridizing a first nucleic acid to a second nucleic acid at least partially complementary to the first nucleic acid, the method comprising:

(1) providing a sample vessel and pressure controller for the vessel;

(2) contacting the first and second nucleic acids within the vessel at a pressure above ambient pressure that is effective to enhance hybridization of the first and second nucleic acids;

(3) further providing a nucleic acid polymerase and at least one nucleotide triphosphate and wherein the first nucleic acid has a 3' terminal nucleotide that hybridizes to an internal nucleotide in the second nucleic acid, the first nucleic acid capable of being extended at least one nucleotide by the polymerase using the second nucleic acid as a template; and

(4) cycling pressure in the vessel between a first higher pressure at which the first and second nucleic acid are hybridized and a second lower pressure at which the first and second nucleic acid are denatured,

wherein a portion of the second nucleic acid is amplified.--

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REMARKS

Claims 1-16 have been cancelled and claims 17-23 have been added. Support for the addition of claims 17-19 can be found, for example, in cancelled claims 1-3 and at pages 21-24 of the specification. Support for the addition of claims 20-22 can be found, for example, in cancelled claims 1-3 and at pages 24-25 of the specification. Support for the addition of claim 23 can be found in cancelled claims 1-3 and 16. The amendment does not add any new matter.

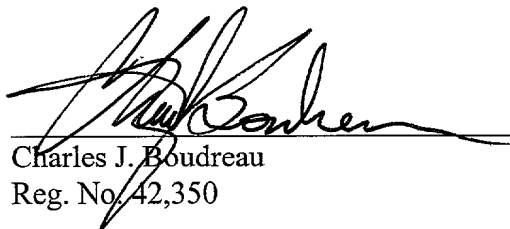
Attached is a marked-up version of the changes being made by the current amendment.

Applicant asks that all claims be examined. Please apply any charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date:

July 9, 2001


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Version with markings to show changes made

In the specification:

Paragraph beginning at page 1, line 6 has been amended as follows:

This application is a continuation of U.S. Application No. 09/035,652, filed March 5, 1998, which claimed the benefit of [claims priority from] U.S. Provisional Application No. 60/076,478 [, entitled "Pressure-Controlled Nucleic Acid Hybridization", Laugharn et al.], filed [on] March 2, 1998, [. A Serial No. for the Provisional Application has not been issued] and of International Application No. PCT/US97/11198, filed July 1, 1997.

In the claims:

Claims 1-16 have been cancelled.

Claims 17-23 have been added as follows:

17. A nucleic acid amplification method, comprising:

- (1) providing a sample vessel and temperature and pressure controllers for the vessel;
- (2) providing a first nucleic acid to be amplified, a nucleic acid primer that is at least partially complementary to the first nucleic acid, a DNA polymerase, and four deoxyribonucleoside triphosphates; wherein the primer has a nucleotide sequence that hybridizes to an internal nucleotide sequence in the first nucleic acid, the primer capable of being extended at least one nucleotide by the polymerase using the first nucleic acid as a template;
- (3) increasing the temperature in the vessel to a temperature effective to cause denaturation of the first nucleic acid;
- (4) increasing pressure in the vessel to a pressure above ambient pressure that allows hybridization between the denatured first nucleic acid and the primer; and
- (5) allowing the DNA polymerase to extend the primer using the denatured first nucleic acid as a template, thereby making a copy of a least part of the first nucleic acid.

18. The method of claim 17, further comprising:

- (6) decreasing pressure to a pressure at which the first nucleic acid again dissociates; and

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(7) repeating steps (4)-(6) to further amplify the first nucleic acid.

19. The method of claim 17, wherein the primer is labelled.

20. A nucleic acid amplification method, comprising:

(1) providing a sample vessel and temperature and pressure controllers for the vessel;

(2) providing a first nucleic acid primer, a second nucleic acid primer, a target nucleic acid to be amplified, and a DNA ligase; wherein the first and second primers are at least partially complementary to the target nucleic acid and hybridize to adjacent sequences on the target nucleic acid;

(3) increasing the temperature in the vessel to a temperature effective to cause denaturation of the target nucleic acid;

(4) contacting the primers and denatured target nucleic acid within the vessel at a pressure above ambient pressure that is effective to allow hybridization between the primers and the denatured target nucleic acid; and

(5) allowing the ligase to ligate the two primers, thereby making a copy of at least part of the target nucleic acid.

21. The method of claim 20, further comprising:

(6) decreasing pressure to a pressure at which the target nucleic acid again dissociates;

and

(7) repeating steps (4)-(6) to further amplify the target nucleic acid.

22. The method of claim 20, wherein the first primer is labelled.

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23. A method of hybridizing a first nucleic acid to a second nucleic acid at least partially complementary to the first nucleic acid, the method comprising:

- (1) providing a sample vessel and pressure controller for the vessel;
 - (2) contacting the first and second nucleic acids within the vessel at a pressure above ambient pressure that is effective to enhance hybridization of the first and second nucleic acids;
 - (3) further providing a nucleic acid polymerase and at least one nucleotide triphosphate and wherein the first nucleic acid has a 3' terminal nucleotide that hybridizes to an internal nucleotide in the second nucleic acid, the first nucleic acid capable of being extended at least one nucleotide by the polymerase using the second nucleic acid as a template; and
 - (4) cycling pressure in the vessel between a first higher pressure at which the first and second nucleic acid are hybridized and a second lower pressure at which the first and second nucleic acid are denatured,
- wherein a portion of the second nucleic acid is amplified.

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